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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,306	04/17/2001	Robert C. Ladner	DYAX/002	9730

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/837,306	LADNER ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-6,21,22 and 37-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-20,23-36 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2, 4/10, 1/15*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on April 23, 2004.

Priority Claims

2. Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 119(e) as follows:

This application claims benefit of 60/198,069 (filed 4/17/2000) (referred to herein as '069). However, the application upon which priority is claimed fails to provide adequate support under 35 U.S.C. § 112 for the claims of this application. Specifically, the '069 application does not provide support for the "genetic package" genus that is currently claimed (e.g., see independent claims 7-9 and 42-44). The '069 provisional application only provides support for phage display (e.g., see 60/198,069 application, page 1, "Area of Invention" section, "The present invention relates to construction of libraries of human Fabs displayed on filamentous phage"). Thus, the '069 provisional application does not provide support for the broader "genetic package" genus that is currently claimed. In support of this position, the Examiner notes that the application also fails to provide support for the vast majority of species that would fall within the scope of the broad and highly variable genetic package genus (e.g., other genetic packages like bacteria, yeast, insect sells, retroviruses, spores, ribosome complexes, etc.

are not disclosed). If applicants believe this to be in error, applicant must disclose where in the specification support for these limitations can be found (i.e., page and line number). In addition, the Examiner does not find support for many of the species of autoimmune disease found in claim 19 (e.g., lupus, erythematosus, systemic sclerosis, vasculitis, etc.). Finally, the Examiner does not find support for many of the species of restriction endonuclease recited in claims 28 and 29 (e.g., Tsp45I, TaaI, MaeIII, HphI, DdeI, BsaJI, etc.).

Therefore the filing date of the instant application is deemed to be its actual filing date of ***April 17, 2001***.

Status of the Claims

3. Claims 1-44 were pending in the present application.

4. Applicant's response to the Restriction and/or Election of Species requirements is acknowledged (Applicant elected ***with traverse*** Group IIII, i.e., claims 7-20, 23-36 and 42-44) and claims 1-6, 21-22 and 37-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see also ***Response to Restriction and/or Election of Species*** below).

5. Please note: Applicant's elected species (Subgroup 1: Species of nucleic acid = single stranded; Subgroup 2: Species of what nucleic acid encodes = FR1; Subgroup 3: Species of autoimmune disease = Lupus; Subgroup 4: Species of isolated cells = Blood cells; Subgroup 5:

Species of amplification = No amplification; Subgroup 6: Species of temperature = 55°C; Subgroup 7: Species of single-stranded oligonucleotide length=20 bases; Subgroup 8: Species of temperature = 55°C; Subgroup 10: Species of length of single-stranded region of double stranded oligonucleotide = 7 bases; Subgroup 11:Species of genetic package = phage) was found in the art. Furthermore, Applicant's *specifically* elected species (Subgroup 9: Species of restriction endonuclease Ms1I) was searched and was not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art, see rejections below. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

6. Therefore, claims 7-20, 23-36 and 42-44 are examined on the merits in this action.

Response to Restriction and/or Election of Species

7. Applicant's election of Group III (claims 7-20, 23-36 and 42-44) is acknowledged (e.g., see 4/23/04 and 11/13/03 Responses). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

8. Applicant's election of species is also acknowledged (e.g., see 4/23/04 and 11/13/03 Responses). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

9. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

10. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

11. The references listed on applicant's PTO-1449 forms have been considered by the Examiner (e.g., 9/2/03; 4/10/02; 1/15/02). A copy of each form is attached to this Office Action.

Specification

12. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Objections to the Claims

13. Claims 12-17 are objected to because of the following informalities:

A. Claims 12-17 are objected to under 37 CFR 1.75(c) as being improper form because a multiple dependent claim depends from another multiple dependent claim. See MPEP § 608.01(n). For compact prosecution claims 12, 14 and 16 are treated as dependent only on claim 10.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 7-20, 23-36 and 42-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a library of phage particles that display antibody fab/scfv wherein said phage particles are produced using class IIs restriction enzymes that cleave the encoding DNA (e.g., see specification, Examples 1-2), is not enabling for the production of any genetic package (i.e., insect, yeast, spore, plant) that expresses any polypeptide/protein (e.g., antibody, receptor, enzyme) using any restriction enzyme (e.g., enzymes that are not class IIs restriction enzymes) to cleave any type of nucleic acid (e.g., RNA). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a broad genus. The scope of these claims includes an almost unlimited number of genetic packages (e.g., bacteria, yeast, insect sells, retroviruses, spores, ribosome complexes, liposome) displaying an almost unlimited number of peptides, polypeptides and/or proteins (antibodies, receptors, enzymes) produced by the cleavage of any nucleic acid with any restriction enzyme. Consequently, the nature of the invention cannot be fully determined.

(3 and 5) The state of the prior art and the level of predictability in the art: A person of skill in the art would not expect all genetic packages (e.g., bacteria, yeast, insect sells, retroviruses, spores, ribosome complexes, liposome) displaying any peptide, polypeptide and/or protein proteins (antibodies, receptors, enzymes) encoded by any nucleic acid (e.g., RNA, DNA, etc.) to behave the same. For example, even within a narrow subset of Applicants' broad claims such as the use of phage display, the art is recognized to be

highly diverse and unpredictable (e.g., see Lowman, H. B.; Wells, J. A. "Affinity Maturation of Human Growth Hormone by Monovalent Phage Display" *J. Mol. Biol.* **1993**, *234*, 564-578, especially page 573, paragraph 3, "The phage display method has important limitations ... For example, not all variants will be displayed on the phage because they may be either digested by proteases, aggregated, misfolded or blocked in secretion or assembly on phage. Although a strong bias against particular DNA sequences is unlikely, there is a clear selection against Cys-containing mutants. This has been previously noted for mutants of hGH (Lowman et al., 1991a) as well as other proteins (Matthews & Wells, 1993) and may be caused by an odd thiol fouling the disulfide bonding scheme in the selected protein binding domain, or in the gene III protein itself which also contains disulfides (van Wezenbeck et al., 1980). Limits in transfection efficiency restrict the number of possible sequences one can screen so one should be selective about the codons randomly mutated"). Here, Applicants' specification provides no guidance on how to protect the displayed proteins from digestion by proteases, aggregation, misfolding, blocked secretion and/or the use of Cys-containing mutants and yet their broad claims encompass such examples.

Another example of the broad and unpredictable nature of the claimed subject matter as exemplified by the prior art would include the use of retroviruses (e.g., see Seed, B "Developments in expression cloning" Current Opinion in Biotechnology 1995, 6: 567-573, especially page 570, column 1, third paragraph "A major problem that has hampered the use of retroviruses as library vectors has been the tendency of viruses with different inserts to exhibit substantially different titers. Thus, preservation of equal

representation in the library, a difficult task even when comparatively simple plasmid-based systems are used, becomes an especially important consideration. At least two potential ways exist in which insert DNA can influence titer in a recombinant retrovirus. The first is based on the unavoidable linkage between RNA expression and titer. If the insert, either as DNA or RNA, confers instability on the viral RNA, or otherwise acts to impede its creation or packaging, the reduced expression directly translates into reduced representation. This is not the case for a plasmid-based libraries, for example, in which reduced expression can make detection of a desired product difficult, but does not, in itself, affect representation. The second is based on the linkage between the efficiency of reverse transcription and titer. If the insert, as RNA, resists reverse transcription (e.g., because it contain extended regions of self-complementarity) this will also result in under-representation. Most RNAs have not been selected for compatibility with the viral life cycle, and so it is not surprising to find wide variation in the efficiency of their reverse transcription in vivo"). Here, Applicants specification provides no guidance with the use of retroviruses and yet their broad claims encompass such embodiments.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants disclose only two examples (e.g., see specification, pages 39-42) wherein DNA is cleaved using Class IIs restriction enzymes to produce a library of DNA sequences that can be subsequently cloned into a PCESI (phagemid vector) vector (e.g., see page 42, line 6). Applicants specification does not provide guidance for other types of genetic packages (e.g., yeast, ribosomes, liposomes, insect, etc.) nor does it

provide guidance for the use of any restriction enzymes other than class IIs restriction sites. Furthermore, not guidance is provided for the use of RNA.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 7-20, 23-36 and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claims 7-9 and 42-44** recite the limitation "the region in which cleavage is desired." There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 7-9, 42-44 and all dependent claims are rejected under 35 USC 112, second paragraph.

B. **Claims 7-9 and 42-44** recite the limitation "the two strands." There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 7-9, 42-44 and all dependent claims are rejected under 35 USC 112, second paragraph.

C. **Claim 10** recite the limitation "the nucleic acids" in the first line. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 10 and all dependent claims are rejected under 35 USC 112, second paragraph.

D. For **claim 7-10, 18, 20 and 42-44**, the term "nucleic acid" and/or "nucleic acids" is vague and indefinite when used in conjunction with oligonucleotide. For example, Applicants use both nucleic acid(s) and oligonucleotide to refer to separate strands of DNA/RNA during, for example, hybridization and/or cleavage processes. However, this use of terminology is confusing because an oligonucleotide is a nucleic acid and, as a result, it is not clear whether Applicants are referring to the same strands of DNA/RNA, separate strands of DNA/RNA or both. For instance, Applicants state in claim 10, "wherein the nucleic acids encode at least a portion of an immunoglobulin." Do Applicants intend this "nucleic acids" to encompass only the "nucleic acid", the

"oligonucleotide" or to both (e.g., compare to claim 7 wherein nucleic acid and oligonucleotide are used to refer only to separate DNA/RNA strands). Thus, Applicants use of terms with overlapping scope in confusing as used throughout the claims. Applicants are requested to clarify and/or correct. Therefore, claims 7-10, 18, 20 and 42-44 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

E. **Claim 7-9 and 42-44** recite the limitation "the oligonucleotide" in step (i). There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 9 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claims Rejections – 35 U.S.C. 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 7-13, 16-20, 23-36 and 42-44 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Suzuki et al. (Suzuki, M.; Takemura, H.; Suzuki, H.; Sumida, T. "Light Chain Determines the Binding Property of Human Anti-dsDNA IgG Autoantibodies" Biochem. Biophys. Res. Commun. **April 29, 2000**, 271, 240-243).

For ***claims 7-13, 16-20, 23-36 and 42-44***, Suzuki et al. disclose a library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and collectively display at least a portion of the diversity of the family (e.g., see abstract wherein genetic package = phage; diverse family of peptides, polypeptides or proteins that is displayed = human anti-double stranded (ds) DNA IgG Fab). Although Suzuki et al. do not disclose that their libraries are formed by the same method steps as recited in claims 7-13, 16-20, 23-36 and 42-44, the products of Suzuki et al. appear to be the same as those recited by the instant claim, regardless of their method of manufacture (e.g., see MPEP 2113) i.e., a genetic package with a diverse family of peptides, polypeptides or proteins is displayed in each case.

For ***claims 10-13, 16, 17***, Suzuki et al. disclose the display of human anti-double stranded (ds) DNA IgG Fab including light/heavy chains (e.g., see abstract).

For ***claims 18-19***, Suzuki et al. disclose Lupus (e.g., see page 240, Materials and Methods, Anti-DNA Fab Clones section, "In brief, total mRNA was isolated from peripheral blood lymphocytes of a patient with lupus nephritis ...").

For ***claim 20***, Suzuki et al. disclose peripheral blood cells (e.g., see page 240, Materials and Methods, Anti-DNA Fab Clones section, "In brief, total mRNA was isolated from peripheral blood lymphocytes of a patient with lupus nephritis ...").

The libraries of Suzuki et al. meet all of the limitations of the claimed library (see above) except for the product-by-process limitations and thus would either anticipate or render obvious the claimed library. See MPEP § 2113, "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product do not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." Here, Applicants claims are drawn to a combinatorial library (i.e., a product), but are defined by various method steps that produce said library and, as a result, represent product-by-process claims. Thus, the process limitations do not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill would expect the library of genetic packages to be the same no matter how it was synthesized and/or prepared.

17. Claims 7-18, 20, 23-36 and 42-44 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Burton et al. (WO 94/07922) (Date of Patent is **April 14, 1994**).

For ***claims 7-18, 20, 23-36 and 42-44***, Burton et al. disclose a library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and collectively display at least a portion of the diversity of the family (e.g., see page 3, Combinatorial Phagemid Libraries Section; see also page 4, lines 6-15, wherein combinatorial libraries of human anti-HIV antibodies are disclosed, "Methods have now been discovered using the phagemid vectors to identify and isolate from combinatorial libraries human monoclonal antibodies that neutralize HIV ..."; see also figures 5 and 15; see also page 41, section F, especially page 42, lines 18-30, "In one embodiment, the method involves preparing a phagemid library of human monoclonal antibodies by using donor immune cell messenger RNA from HIV infected donors ... Alternatively, the library can be synthetic, or can be derived from a donor who has an immune response to other antigens"). Although Burton et al. do not disclose that their libraries are formed by the same method steps as recited in claims 7-18, 20, 23-36 and 42-44, the products of Burton et al. appear to be the same as those recited by the instant claim, regardless of their method of manufacture (e.g., see MPEP 2113) i.e., a genetic package with a diverse family of peptides, polypeptides or proteins is displayed in each case.

For ***claims 10-17***, Burton et al. disclose the display of human antibodies with light/heavy chains including Fab and FR1 regions (e.g., see page 43, lines 19-23, "For example, the heavy (H) chain and light (L) chain immunoglobulin molecule encoding genes can be randomly mixed (shuffled) to create new HL pairs in an assembled immunoglobulin molecule"; see also page 44, lines 9-13, "In addition, the monoclonal antibodies are human because the H and L chain encoding genes are derived from human immunoglobulin producing immune cells, such as spleen, thymus, bone marrow, and the like"; see also figures 6-13 wherein recombinant Fabs are disclosed; see also figure 10 wherein FR1 is disclosed).

For ***claims 18***, Burton et al. disclose acquired autoimmuno-deficiency syndrome (e.g., see page 18, lines 3-4).

For ***claim 20***, Burton et al. disclose spleen, bone marrow, etc. (e.g., see page 42, lines 18-30, especially lines 28-30, "Alternatively, the library can be ... derived from a donor who has an immune response to other antigens"; see also page 44, lines 9-13, "In addition, the monoclonal antibodies are human because the H and L chain encoding genes are derived from human immunoglobulin producing immune cells, such as spleen, thymus, bone marrow").

The libraries of Burton et al. meet all of the limitations of the claimed library (see above) except for the product-by-process limitations and thus would either anticipate or render obvious the claimed library. See MPEP § 2113, "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product do not depend on its method of

production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." Here, Applicants claims are drawn to a combinatorial library (i.e., a product), but are defined by various method steps that produce said library and, as a result, represent product-by-process claims. Thus, the process limitations do not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill would expect the library of genetic packages to be the same no matter how it was synthesized.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 7-20, 23-36 and 42-44 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-116 of copending Application No. 10/045,674 (Pub. No.: US 2003/0232333 A1) (referred to herein as

'674). Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). For example, claims 7-20, 23-36 and 42-44 of the present application represent overlapping embodiments to all that is recited in claims 1-116 of '674. That is claims 1-116 of '674 either anticipate or render obvious the claims of the present application.

Specifically, both applications claim **[1]** a library comprising a collection of genetic packages (e.g., compare claim 7 of the present application to claims 11-13, 17, 18, 59, 62, 103, 114 of '674, especially claim 12), **[2]** genetic packages that display a member of a diverse family of peptides polypeptides or proteins wherein at least a portion of the diversity of said family is displayed (e.g., compare claim 7 of the present application to claims 11, 12, 13, 59, 62, 103, 114 of '674, especially claim 12), **[3]** displayed peptides, polypeptides, or proteins being encoded at least in part by a nucleic acid that has been cleaved at a desired location (e.g., compare claim 7 of the present application to claims 3, 4, 12, 13 and 99 of '674, especially claim 12), **[4]** contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired (e.g., compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 54, 59, 60, 99-104 and 108 of '674, especially claim 12), **[5]** including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location (e.g., compare claim 7 of the present application to claims 1,

3, 5, 7, 9, 12, 15, 59, 60, 103 and 104 of '674, especially claim 12), **[6]** cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid (e.g., compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 59, 60, 103 and 104 of '674, especially claim 12), **[7]** the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form (e.g., compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 54, 59, 60, 99-104 of '674, especially claim 12), **[8]** the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location (e.g., compare claim 7 of the present application to claims 1-13, 15, 16, 54, 59, 60, 99-104 of '674, especially claim 12). Finally, both applications also disclose the cleavage site being carried out using a restriction endonuclease that is active at the chosen temperature (e.g., compare claim 7 of the present application to claims compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 54, 59, 60, 99-104 of '674, especially claim 12). Thus, claim 7 of the present application is anticipated by claim 12 of '674 and overlaps in scope with the other claims as outlined above.

In addition, both applications disclose **[9]** the use of "DNA sequences" to encode the diverse family of displayed peptides, polypeptides or proteins (e.g., compare claim 8 of the present application to claims 12, 13, 15 and 16 of '674), **[10]** contacting the nucleic acid with a partially double-stranded oligonucleotide (e.g., compare claim 9 of the present application to claims 2, 4, 6, 8, 10, 13, 16, 54, 59, 60, 99-104, 108 of '674), **[11]** the use of Type II-S cleavage sites (e.g., compare claim 9 to claims 19, 52 and 53 of '674), **[12]** the use of immunoglobulins (e.g., compare claim 10 of the present application to claims 21, 22, 23, 26, 28, 36, 65, 75, 92 and

94 of '674), **[13]** Fab or single chain Fv (e.g., compare claim 11 of the present application to claims 22 and 70 of '674), the use of the heavy chain (e.g., compare claim 12 of the present application to claims 23, 24, 25, 68, 71, 80, 81 of '674), **[14]** human FR1 (e.g., compare claims 14 and 15 of the present application to claim 27 of '674), **[15]** the use of a light chain (e.g., compare claim 16 of the present application to claims 28, 29, 67, 70, 82 and 83 of the present application), **[16]** wherein the nucleic acid sequences are at least in part derived from patients suffering from at least one autoimmune disease (e.g., compare claim 19 of the present application to claims 30, 31 and 85 of '674), **[17]** including diseases like lupus (e.g., compare claim 19 of the present application to claim 31 of '674), **[18]** nucleic acid that is isolated, for example, by peripheral blood cells (e.g., compare claim 20 of the present application to claim 32 of '674), **[19]** a temperature between 55 and 60°C (e.g., compare claims 23-25 of the present application to claims 39-42 of '674), the length of the single-stranded oligonucleotide between 17 and 30 bases (e.g., compare claims 26-27 of the current application to claims 43, 44, 49, 55, 56, 109 and 110 of '674), **[20]** the use of endonucleases like BsaJI 9 (e.g., compare claim 28 of the present application to claim 45 of '674), **[21]** the use of partially double-stranded oligonucleotide between 18 and 20 bases (e.g., compare claims 30-32 of the present application to claims 47, 48, 50, 51, 55-58 and 109-112 of '674) and **[22]** partially double stranded region formed by stem and its palindrome (e.g., compare claim 33 of the present application to claims 50 and 52 of '674).

Furthermore, it would have been obvious to one having ordinary skill in the art to modify embodiments of '674 that fall outside the scope of the present application to select a specifically disclosed embodiment that falls within the scope of the present application because these

embodiments describe similar and/or identical libraries. One having ordinary skill in the art would have been motivated to do this because these embodiments are disclosed as being preferred embodiments and the dependent claims of '674 teach toward Applicants' claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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